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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/965,640	09/27/2001	John E. Sims	0315-C	3481

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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	**PAPER NUMBER**
1646	10

DATE MAILED: 02/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/965,640	SIMS, JOHN E.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-12 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-12 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5, 6 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the claims

1. Claims 1 and 4-9 have been amended and claims 10-12 have been added as requested in the amendment of paper No. 9, filed on November 25, 2002. Claims 1-12 are pending in the instant application.

Election/Restrictions

2. Applicant's election without traverse of Group I in Paper No. 9 is acknowledged.

Group I, claims 1-9, is directed to a method of treating an individual by administration of an IL-1 delta polypeptide of SEQ ID NO: 2. Preliminary examination indicated that claims 1-12, as amended, are directed to invention of Group II, which is a method of treatment by administration of an IL-1 delta of SEQ ID NO: 4. A telephone call was made to contact Applicant's representative, Anne Perkins, on January 28, 2003 to clarify Applicant's election. During the telephone conversation it was confirmed that Applicant's intention was to elect an invention of Group II, drawn to method of treating an individual by administration of an IL-1 delta polypeptide of SEQ ID NO: 4.

Claims 1-12 are under examination in the instant office action.

Sequence compliance

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825. Specifically, no sequence listing has been provided which includes sequences presented

on page 16, lines 2-3 and 5-6 and pages 42 and 43 of the instant specification. Applicant needs to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. §§ 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. For rules interpretation Applicant may call (703) 308-1123. See M.P.E.P. 2422.04.

Specification

4. Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;

(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) if a process, the steps.

Applicant's attention is directed to section (5) above.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

6. The text of the instant specification does not comply with 37 C.F.R. 1.52 (b) with respect to font size.

37 C.F.R. 1.58 (b) states that:
(b) The application (specification, including the claims, drawings, and oath or declaration) or reexamination proceeding and any amendments or corrections to the application or reexamination proceeding .
(1) The application or proceeding and any amendments or corrections to the application (including any translation submitted pursuant to paragraph (d) of this section) or proceeding, except as provided for in § 1.69 and paragraph
(d) of this section, must:
(i) Comply with the requirements of paragraph (a) of this section; and
(ii) Be in the English language or be accompanied by a translation of the application and a translation of any corrections or amendments into the English language together with a statement that the translation is accurate.
(2) The specification (including the abstract and claims) for other than reissue applications and reexamination proceedings, and any amendments for applications (including reissue applications) and reexamination proceedings to the specification, except as provided for in §§ 1.821 through 1.825, must have:
(i) Lines that are 1 1/2 or double spaced;
(ii) Text written in a nonscript type font (e.g., Arial, Times Roman, or Courier) lettering style having capital letters which are at least 0.21 cm (0.08 inch) high; and
(iii) Only a single column of text.

7. The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code, see pages 26 and 43, for example. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The use of the trademarks has been noted in this application, see page 45, for example. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant is advised to review the entire text of the instant specification for other possible use of trademarks or hyperlinks.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

Claims 1-12 are directed to a method of treating an individual afflicted with an inflammatory and/or autoimmune disease by administration of a human IL-1 delta polypeptide. The instant application has provided a description of an isolated DNA encoding an IL-1 delta protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance. Because the biological significance of the IL-1 delta of the instant invention is not disclosed, one skilled in the art clearly would not know how to use IL-1 delta.

It is clear from the instant application that the protein encoded by the isolated nucleic acid molecule described therein is what is termed an "orphan protein" in the art. The DNA of the

instant application has been isolated because of its similarity to a known DNA. There is little doubt that, after complete characterization, this DNA and encoded protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The instant claims are drawn to a method of treating an individual afflicted with an inflammatory and/or autoimmune disease by administration of a human IL-1 delta polypeptide. However, the specification does not disclose the function or biological significance of that IL-1 delta protein. It is clear from the instant application that novel IL-1 delta of the instant invention shows structural similarity to IL-1 class of cytokines, such as "[h]uman IL-1 delta polypeptide exhibited little identity with IL-1α, 29% identity with IL-1β, 50% identity with IL-1ra, little

identity with IL-18, 31% identity with IL-1 epsilon, and 34% with IL-zeta" (page 5, lines 39-40 and page 6, line 1 of the instant specification). The pattern of tissue distribution of IL-1 delta was identified as follows "[h]uman IL-1 delta RNA expression can be detected in lymph node, thymus, tonsil, brain, placenta, lung, skeletal muscle, prostate, and testis" (page 5, lines 21-22). Because of the structural similarity of the instant IL-1 delta to other IL-1 polypeptides and IL-1 ra (IL-1 receptor antagonist) in particular, it was asserted that IL-1 delta of the instant invention would possess the same activity and have the same function as IL-1 ra. Numerous publications exist on a topic of predicting protein functions from structural similarities or homology to the known proteins. It is well described in the art that amino acid structure cannot necessarily predict the function of the protein: "Knowing the protein structure by itself is insufficient to annotate a number of functional classes and is also insufficient for annotating the specific details of protein function" (see Skolnick et al., Box 2 on page 36 and the whole paper). Moreover, "Structural similarity does not necessarily mean a common evolutionary origin and homologous sequences may evolve into different folds (according to current classification schemes) (See Bork et al., Current Opinion in structural Biology, 1998, 8, page 332, first column, second paragraph). Thus, according to the state of the art, functional characteristics of a protein cannot be unequivocally extrapolated from its structural characteristics.

In the absence of knowledge of the biological significance of this specific IL-1 delta protein, one skilled in the art would not reasonably expect that administration of IL-1 delta to an individual would result in any particular effect. Therefore, there is no immediately obvious patentable use for a method of administration of IL-1 delta to treat any disease or a pathological condition. According to the specification of the instant application "administration of IL-1 delta

will have therapeutic application in blocking inflammatory responses" (page 30, last paragraph of the instant specification) and "IL-1 delta will be useful in treating arthritic conditions that have an inflammatory or autoimmune component, for example, rheumatoid arthritis and/or ankylosing spondylitis; inflammatory bowel disease, including Chron's Disease and ulcerative colitis, and psoriasis" (page 31, second paragraph). The instant specification fails to provide any evidence or sound scientific reasoning that would support a conclusion that the instant IL-1 delta is associated with any diseases or disorder. Because the instant specification does not teach a biological activity of the protein, which supports a practical utility, one would not reasonably believe that the administration of the claimed peptide would prevent or treat a condition or disease, including diseases listed on page 31, second paragraph and in claims 3 and 12, as implied by the specification.

To employ IL-1 delta of the instant invention in a method of treating an individual afflicted with inflammatory or autoimmune disease would clearly be using it as the object of further research, which clearly requires one skilled in the art to partake in a substantial amount of undue experimentation in order to practice Applicant's invention as currently claimed.

9. Claims 1-9 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-9 are directed to a method of treating an individual afflicted with an inflammatory and/or autoimmune disease by administration of a IL-1 delta polypeptide encoded by DNAs that hybridize to the DNA of SEQ ID NO: 3 or by administration of polypeptides that

are 80% identical to the polypeptide of SEQ ID NO: 4 wherein the polypeptides block an inflammatory response. However, the instant specification fails to describe the entire genus of proteins, which are encompassed by these claims. In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of a nucleic acid molecule which encodes a protein which has the amino acid sequence of SEQ ID NO: 4. This nucleic acid molecule has a nucleic acid sequence of SEQ ID NO: 3. The subject matter which is claimed is described above. First, a determination of the level of predictability in the art must be made in that whether the level of skill in the art leads to a predictability of structure; and/or whether teachings in the application or prior art lead to a predictability of structure. The claims encompass a method of treating an individual afflicted with an inflammatory and/or autoimmune disease by administration of a IL-1 delta polypeptide encoded by DNAs that hybridize to the DNA of SEQ ID NO: 3 or by administration of polypeptides that are 80% identical to the polypeptide of SEQ ID NO: 4 wherein the polypeptides block an inflammatory response. First, the claims are not limited to a method of treatment by administration of a protein with a specific amino acid sequence. The claims only require the polypeptide share some degree of structural similarity to the isolated protein of SEQ ID NO: 4. The specification only describes a protein having the amino acid sequence of SEQ ID NO: 4 and fails to teach or describe any other protein which lacks the amino acid sequence of SEQ ID NO: 4 and has the activities possessed by the isolated protein. Therefore, there is a lack of guidance or teaching regarding structure and

function because there is only a single example provided in the specification and because there is no guidance found in the prior art.

Next in making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, each claimed species and genus must be evaluated to determine whether there is sufficient written description to inform a skilled artisan that applicant was in possession of the claimed invention at the time the application was filed. With this regard, the instant application fails to provide a written description of the species or the genus which are encompassed by the instant claims except for the protein of SEQ ID NO:1. The specification does not provide a complete structure of those polypeptides which are encoded by DNAs that hybridize to the DNA of SEQ ID NO: 3 or are 80% identical to the polypeptide of SEQ ID NO: 4 wherein the polypeptides possess the function of being able to block an inflammatory response. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. The specification fails to provide a representative number of species for the claimed genus (those proteins which are encoded by DNAs that hybridize to the DNA of SEQ ID NO: 3 or are 80% identical to the polypeptide of SEQ ID NO: 4 wherein the polypeptides possess the function of being able to block an inflammatory response) because the specification teaches only the one embodiment of SEQ ID NO: 4. Therefore, the claims are directed subject matter which was not described in the

specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claim 1 is indefinite and ambiguous for recitation of hybridization "under moderately stringent conditions". Without providing a precise set of hybridization conditions, in the claim or the specification, the metes and bounds of the claimed isolated nucleic acid molecule cannot be defined.

12. Claims 3 and 12 are indefinite because the recited therein diseases do not appear to belong to the group of "an inflammatory and/or autoimmune disease". Recitation "and/or" encompasses both "an inflammatory and autoimmune disease" and "an inflammatory or autoimmune disease". Therefore, it is not clear how, for example, heat stroke or sepsis can be included in the group of "an inflammatory and autoimmune disease".

Claims 3 and 12 are further vague and indefinite for recitation "combinations thereof". It is not clear how many different combinations of all the recited disease are indented to be treated by administration of IL-1 delta.

13. Claims 4, 5 and 6 are vague and ambiguous for reciting "variant amino acid sequence". The metes and bounds of the recitation cannot be determined form the claims. Is it a variant sequence or variant sequences? Clarification id required.

14. Claims 7-9 are indefinite because recitation "selected from the group consisting of " is used twice in one sentence and appears to describe only one group of polypeptides. It is suggested that the claims are rewritten to better articulate the claimed subject matter. Further, the metes and bounds of "inactivated [...] site" are not clear and not defined in the claims or the instant specification, which renders the claims indefinite.

15. Claim 2 is indefinite for being dependent form the indefinite claim.

Conclusion

16. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax

center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.
February 4, 2003

JOHN ULM
PRIMARY EXAMINER
GROUP 1800